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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/716,169	12/17/1996	STEPHEN M. ANDERTON	961125	5487

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

MAIL DATE	DELIVERY MODE
08/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/716,169	ANDERTON ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-26 and 28-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-26 and 28-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 5/29/07 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment and remarks, filed 5/29/07, have been entered.

2. Claims 24-26 and 28-32 are being acted upon.

3. Applicant's amendment and remarks, filed 9/16/06, are acknowledged. In view of Applicant's amendment and remarks, all previous rejections have been withdrawn.

4. The following are new grounds for rejection.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 24-26 and 28-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the method of the instant claims would function as claimed.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention,

see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

A review of the specification reveals only that preimmunization of Lewis rats with a peptide consisting of *M. tuberculosis* hsp65 86-100 provided a barely noticeable reduction in adjuvant-induced arthritis (AA) severity, and preimmunization of Lewis rats with a peptide consisting of *M. tuberculosis* hsp65 256-270 provided a more substantial reduction in both AA and CP20961-induced arthritis severity. It is unclear how these minimal showings can enable a method of treating *all* Th1-mediated inflammatory diseases in *all* species including humans.

First note that *no* treatment whatsoever of *any* disease is disclosed. It is well-established that preimmunization to prevent or reduce the severity of many diseases can be effective whereas actual treatment of established disease is not, e.g., rabies or experimental prevention of other autoimmune diseases such as diabetes and EAE. Also note that the specification at page 28 teaches that the reduction in severity of AA is absolutely MHC dependant, i.e., RT1.D^1 restricted. Accordingly, it is unclear how this treatment could be expected to work in the outbred human population whose MHC differences vary significantly more than do the Lewis rat's. Further note that the peptides of the instant claims, *M. tuberculosis* hsp65 81-100 and 241-270 are not even the peptides of the examples, i.e.,

they are larger. Given that the claims encompass the use of peptides comprising as few as 5 amino acids of *M. tuberculosis* hsp65 81-100 or 241-270, a peptide comprising, for example, hsp65 241-246 (for which there has been no showing of any sort of efficacy) might be encompassed for use in the method of the instant claims (if it could be shown that the fragment had a "corresponding mammalian stress protein homologue").

Also note that the mechanism by which the claimed method would function was not well understood. Indeed, the discussion at pages 27-28 discloses only that, "the hypothesis is that the mechanism by which hsp65 preimmunisation protects Lewis rats against arthritis is based on activation of T cells that recognise an epitope shared with rat hsp60. Recognition by these T cells of elevated levels of the self epitope presented by MHC class II expressing cells at the site of inflammation (the joint) would then provide an antigen-specific mechanism for regulation of the inflammatory process." There is no discussion of the induction of T regulatory cells which the Inventors now argue is the invention. Finally, the specification provides no reason why the method of the instant claims would be expected to be effective against any and all Th1-mediated inflammatory diseases.

Regarding the use of APLs for the treatment of autoimmune disease, Anderton (2001, of record), teaches that,

> "This unpredictability [of APLs] led us to argue against the use of antagonist or immune deviating APL in human autoimmune disorders" (page 370).

The reference goes on to teach that APL administration to humans can be dangerous and that in at least one case a human trial was suspended due to adverse reactions in a significant number of patients. Note that this is one of the Inventors' own work. While it might be argued that the hsp65 peptides of the instant claims are not APLs *per se*, the peptides administered in the claimed method require only a 5 amino acid identity with *M. tuberculosis* hsp65, thus from 2-25 amino acids may vary. In this case the peptides would indeed functionally comprise APLs.

As set forth in *Rasmusson v. SmithKline Beecham Corp.*, 75 USPQ2d 1297, 1302 (CAFC 2005), enablement cannot be established unless one skilled in the art "would accept without question" an Applicant's statements regarding an invention, particularly in

the absence of evidence regarding the effect of a claimed invention. Specifically:

> "As we have explained, we have required a greater measure of proof, and for good reason. If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to "inventions" consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the "inventor" would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis."

Thus, in view of the quantity of experimentation necessary, the lack of sufficient guidance in the specification, the lack of sufficient working examples, i.e., the specification discloses no data representative of the broad method of the instant claims, the unpredictability of the art, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

7. Claims 24-26 and 28-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Under *Vas-Cath, Inc. v. Mahurkar* , 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention, and that the invention, in that context, is whatever is now claimed.

There is insufficient written description to show that Applicant was in possession of "a peptide of 7-30 amino acids having the sequence of a part of the amino acid sequence of a mycobacterial protein having a conserved mammalian stress protein homologue, said part comprising at least 5 amino acids which are identical with the corresponding amino acids in the same relative position in one of the sequences 81-100 and 241-270 of SEQ ID NO.

1 representing the sequence of the stress protein hsp65 of *Mycobacterium tuberculosis*, at least 4 consecutive amino acids of said at least 5 amino acids being identical with the corresponding mammalian stress protein amino acids amino acids". Note that while the peptides employed in the claimed method are fragments of SEQ ID NO:1, to establish which fragments are encompassed for use in the instant claims their "corresponding" "mammalian stress protein homologues" must be described.

An adequate written description of the peptides employed in the method of the claims would require either an adequate description of a common function *and* structure, or a disclosure of a representative number of species. A review of the definition of "stress proteins" at page 2 of the specification shows that they encompass "enzymes or proteins that exhibit a raised level of synthesis during inflammation or other stress stimuli in cells residing at the site of such inflammation or stress condition", including heat shock proteins, interleukins and interferons. While some attempt is made at disclosing a common cause of induction, no common structural or functional features are disclosed. Indeed, it is well-established that heat shock proteins and interleukins do *not* share a common structure or function. Given these facts, one of skill in the art would conclude that the specification fails to disclose either a representative number of species (just one, *M. tuberculosis* hsp65 241-270 presumably corresponding to human hsp65) or common functional and structural characteristics, adequate to describe the peptides required for use in the method of the instant claims. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

8. Claims 24-26 and 28-32 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, a method of treatment of a Th1-mediated [disease] comprising ... administering an effective amount of a peptide of 7-30 amino acids having the sequence of a part of the amino acid sequence

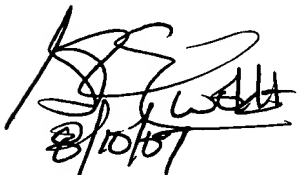
of *M. tuberculosis* … said part comprising at least 5 amino acids which are identical with the corresponding amino acids … at least 4 consecutive amino acids of said 5 amino acids bind identical with the corresponding mammalian stress protein amino acids (Claim 24).

First note that neither Th1-mediated disease nor a peptide of 7-30 amino acids has been found in the specification. Further, while bits and pieces of the claim might be found throughout the specification, no support for the specific combination of limitations set forth in the method of Claim 24 has been found.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571)272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571)272-0841.

11. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see www.pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)217-9197.



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